190709-4). Formal written informed consent was not required because of the retrospective nature of the study, which used anonymized data generated from our regular practice.

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A SARS-CoV-2-positive patient coincidentally diagnosed with B-ALL

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Key words B-ALL, chemotherapy, COVID-19, SARS-CoV-2.

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) infection, is now a pandemic. Patients who are elderly, immunocompromised, or have comorbidities such as diabetes and hypertension, are at high-risk of COVID-19 mortality. Children are regarded as low-risk because severe respiratory failure occurred in only three among 171 cases (1.75%) in the beginning of 2020 in China.[1] Severe COVID-19 cases in children have seldom been reported, even for individuals with childhood cancer or leukemia.[2] Here, we report a SARS-CoV-2-positive girl coincidentally diagnosed with acute B-cell acute lymphoblastic leukemia (B-ALL).

A previously healthy 6-year-old girl complained of back pain and gradually became dysstatic. After 2 weeks she developed additional symptoms, (e.g., paresthesia, remittent fever, and nasal bleeding), requiring hospital admission. On admission (day 1), her laboratory findings revealed pancytopenia: white-blood-cell count of 3.77×10^9 cells/L, neutropenia (0.3×10^9 cells/L), anemia (Hb, 7.0 g/dL), thrombocytopenia (17×10^9 cells/L), and elevated lactate dehydrogenase (952 IU/L) and uric acid (6.8 mg/dL) levels. C-reactive protein was also detected (4.55 mg/dL). No hepatomegaly or lymphadenopathy was observed. Piperacillin-tazobactam administration was started from day 1; however, because her blood culture was positive for *Staphylococcus aureus*, the antibiotic treatment was changed to meropenem from day 2. The nasopharyngeal swab sample was SARS-CoV-2-positive by real-time polymerase chain reaction (PCR) and favipiravir administration was started from day 2. Radiography showed a thoracolumbar vertebral compression fracture that was responsible for her neurological symptoms. However, computed tomography (CT) of the lungs showed no abnormal finding suggestive of pneumonia. Her mother was SARS-CoV-2 PCR-negative; the other family members were not tested. Abnormal lymphoblasts emerged in her peripheral blood and acute leukemia was suspected. She was transferred to our hospital on day 8, where she and her mother were isolated in special wards for SARS-CoV-2-infected patients.

On day 15, the patient had her first SARS-CoV-2 PCR-negative result, and a follow-up examination on day 17 also yielded negative results. She was then transferred to the pediatric ward. Bone marrow examination revealed 100% of lymphoblasts as positive for CD10, 19, 20, 22, 34, 58, cytoplasmic CD79a, KORSA-3544, HLA-DR, cytoplasmic Igμ, and terminal deoxynucleotidyl transferase. Chimeric gene screening was negative and the chromosomal analysis showed a normal karyotype.

Prednisolone administration began on day 32, and her response was good. On day 46, a follow-up SARS-CoV-2 PCR was negative, and she showed no COVID-19 symptoms during induction chemotherapy for B-ALL. She achieved complete remission after induction therapy. Her clinical and therapeutic course is shown in Figure 1.

Patients with ALL commonly show an immunosuppressed status at diagnosis, and infections such as bacteremia, respiratory tract infection, viral infection, and fungal infection are

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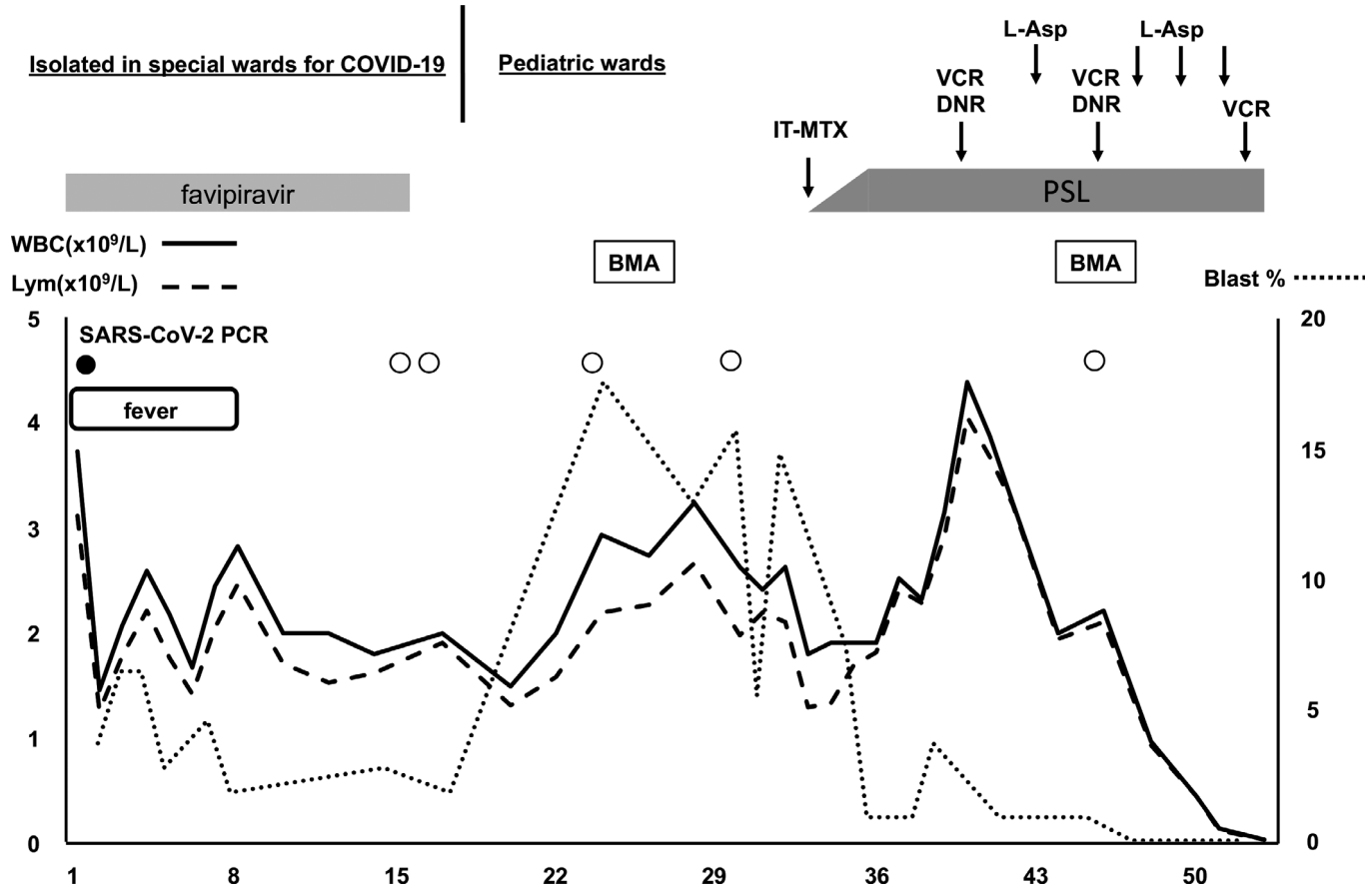

Fig. 1 Clinical and therapeutic course of this patient. The closed circles and open circles represent SARS-CoV-2 polymerase chain reaction-positive and -negative, respectively. Anti-bacterial agents and transfusion are not shown. BMA, bone marrow aspiration; DNR, daunorubicin; IT-MTX, intrathecal injection of methotrexate; L-Asp, L-asparaginase; Lym, lymphocytes; PSL, prednisolone; VCR, vincristine. WBC, white blood cells.

major causes of death during remission induction chemotherapy. Our patient's case was complicated by staphylococcus bacteremia and SARS-CoV-2 infection at the time of B-ALL diagnosis. We repeatedly confirmed PCR-negative status to avoid worsening of the SARS-CoV-2 infection because there are some cases that become PCR-positive again after having been negative once. In addition, she could become a super-spreader following chemotherapy and corticosteroids use. So, we decided to perform a bone marrow examination and delayed chemotherapy. Fortunately, she tolerated almost 30 days of only supportive therapy because the abnormal lymphoblast proliferation was indolent, and the residual neutrophils and suitable antibiotics were able to resolve the bacteremia. Favipiravir, a polymerase inhibitor developed for treating influenza, has been used for treating COVID-19 in Japan; however, its effect against COVID-19 is still under evaluation in clinical trials. Here, the relatively high amounts of normal lymphocytes in her peripheral blood might have contributed to clearing the SARS-CoV-2 virus. By postponing chemotherapy, we successfully prevented COVID-19 in this case.

Although severe respiratory failure in an 8-year-old Chinese boy with T-cell ALL (T-ALL) has been reported, the details are not published in English. A French group discussed what to do if an ALL patient is diagnosed with SARS-CoV-2 infection.[3] They recommended the ceasing and/or postponing of all chemotherapies, according to the ALL severity. We were able to safely manage our patient by postponing the induction chemotherapy because she had low-risk ALL, with no hyperleukocytosis, renal dysfunction, or disseminated intravascular coagulation. Corticosteroid use for treating COVID-19 is still controversial.

Pediatric patients with laboratory-confirmed COVID-19 tend to have mild or asymptomatic cases, even when they are immunocompromised[4]; however, precautions should still be taken to prevent COVID-19. In a recent report, 30% of pediatric patients with laboratory-confirmed COVID-19 showed no clinical manifestation and had negative chest CT findings.[5] Therefore, laboratory-confirmed COVID-19 is not equal to COVID-19, and the infectivity of such cases is still unknown. Further information on cases of COVID-19 in patients with childhood cancers is needed.

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Disclosure

The authors declare no conflict of interest.

Author contributions

M.Y., Y.A., K.I., and T.H. treated the patient. M.Y. and Y.K. wrote the manuscript. All authors read and approved the final manuscript.

Informed consent

Written informed consent to publish the findings was obtained from the patient's mother.

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A useful method to diagnose Pearson syndrome mimicking Diamond–Blackfan anemia

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Key words Diamond–Blackfan anemia, extracellular flux analyzer, mitochondrial oxidative phosphorylation, Pearson syndrome.

Pearson syndrome (PS) is a multisystem disorder characterized by hematological abnormalities (transfusion-dependent anemia, neutropenia, or thrombocytopenia), exocrine pancreatic dysfunction, and lactic acidosis. All symptoms are caused by mitochondrial DNA (mtDNA) deletions. At approximately one case per million, the incidence is extremely rare. Most infants with this condition die before 3 years of age.[1] The establishment of an appropriate diagnosis of PS in newborns is often difficult because its clinical features usually overlap with other common diseases, and typical bone marrow features, such as vacuolization in hematopoietic progenitors and ringed sideroblasts, may be entirely or partially lacking.[2] Diamond–Blackfan anemia (DBA) is characterized by severe hyporegenerative macrocytic anemia, congenital malformations, and growth retardation. In 50–60% of these patients, mutations affecting the ribosomal proteins or *GATA1* gene are identified. Diamond–Blackfan anemia occurs more frequently than PS, with an estimated incidence of one to two cases per 100 000. Diamond–Blackfan anemia and PS share several features including early onset of severe anemia, variable nonhematologic manifestations, sporadic genetic inheritance, and episodes of spontaneous hematologic improvement. Gagne *et al*. evaluated DNA samples from the patients who were diagnosed with DBA and found 8 of 173 (4.6%) had large mtDNA deletions indicating misdiagnosis.[3] We report the case of a patient with PS mimicking DBA who was immediately diagnosed by impaired mitochondrial oxidative phosphorylation (OXPHOS) in peripheral blood (PB) and bone marrow (BM) mononuclear cells prior to the confirmation of mtDNA deletion.

The patient was born at full-term, with a birthweight of 2,476 g following an uncomplicated pregnancy with severe anemia (Hb 2.6 g/dL) and lactic acidosis (4–10 mmol/L). Monthly red blood cell transfusions were necessary to maintain the hemoglobin level. Targeted exome sequencing, including the ribosomal proteins, *GATA1* gene, and mitochondrial

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